The Christ Hospital IRB
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IRB REFERENCE MANUAL
SECTION 16
INFORMED CONSENT

16.0 INFORMED CONSENT

16.1 Informed Consent for Human Subject Research

A. Ethical Foundation

Informed consent is one of the primary ethical considerations in research involving human participants. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research describes the purpose of consent as the mechanism to ensure that participants understand the research study and voluntarily agree to participate. A copy of the Belmont Report may be found here.

The PI and study team members should consider that consent is a process, and not just a form that potential study participants must sign.

B. Regulatory requirements for informed consent

There are federal requirements that mandate the type of consent that may be obtained, the elements that should be present in a consent explanation, and who may obtain and give consent for research purposes. Below is an outline of these requirements.

Federal Requirements: Informed consent must meet the regulatory requirements of the US Department of Health and Human Services (45 CFR 46.116) and the US Food and Drug Administration (21 CFR 50.20). Under these regulations, there are six general requirements for informed consent:

1) Consent Required: Investigators may involve human participants in research only with the consent of the participant or his/her legally authorized representative, unless the requirement for consent is waived. There are exceptions for waiver of consent, but waivers are highly regulated and must be justified. (see: http://irb.jhmi.edu/Guidelines/WaiverorAlterationofInformedConsent)

2) Voluntary Participation: The potential study participant must be given enough time to consider whether or not to participate in the research, and

the possibility of coercion or undue influence should be minimized.

3) Understandable Language: Consent explanations must be in language understandable to the potential study participant or the individual's legally authorized representative.

4) Waiver of Rights Prohibited: The consent may not include language through which the participant or their representative is made to waive the participant's legal rights or releases the investigator, the sponsor, the institution or its agents from liability for negligence.

5) Key Information: Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

6) Organized to Assist Understanding: Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.

Please note: While 45 CFR 46.116(a) permits a broad consent, which may be obtained with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens, TCH IRB will not approve a broad consent process.

16.2 The Informed Consent Process

Under the federal regulations, a PI must obtain "legally effective" informed consent in order to enroll a person into a research study. The "consent process" describes who will obtain informed consent and from whom, and when, where and how the consent process will take place. It also involves an assessment by the consent designee that the person providing informed consent understands what is being asked of him/her. Informed consent is legally effective if:

1. it is obtained from the subject or the subject's legally authorized representative; and
2. it is documented in a manner that is consistent with the federal regulations on protection of human subjects (DHHS, FDA) and with the applicable laws of the jurisdiction in which the research is conducted, and
3. it is obtained under circumstances that:

- provide the prospective subject or the legally authorized representative sufficient opportunity to consider whether to participate in the research;
- minimize the possibility of coercion or undue influence, and
- respects the privacy of the potential participant by taking place in a setting that is not open to the public

The information provided should be in language that is understandable to the subject or the representative. No informed consent may include any exculpatory language (language that waives or appears to waive any of the participant's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence).

The regulations provide two possible mechanisms for obtaining informed consent from a research participant:

- a process with consent documented by having the appropriate person sign a written IRB approved consent document, or
- a process involving a waiver of documentation of consent that has been approved by the IRB.

A. Process for Obtaining Informed Consent Documentation

Generally, the IRB requires consent to be documented by a written consent form that includes all the required elements, and all appropriate optional elements, approved by the IRB prior to use. An IRB approved consent document will contain the date of IRB approval. Unless the need for consent is waived by the IRB, the written consent form must be reviewed with the participant (or the participant's representative), and signed and dated by the participant or the participant's representative before any research procedures (including screening) or research data collection can begin. The consent form should also be signed and dated by the individual who obtains the participant's consent.

B. Waiver or Alteration of Informed Consent

Per federal regulations 45 CFR 46.116, a waiver of one or more elements of consent is permitted provided that the research is no more than minimal risk and meets specific criteria. Alteration of consent is appropriate if one or more of the 8 required elements is not relevant to the research activity. Complete waiver of consent is also permitted; this is most frequently granted for retrospective research but is also possible for some types of prospective research. However, FDA regulations do not permit waiver or alteration of consent for FDA-regulated research.

The investigator should submit this request for waiver or alteration of consent with the study application.

The IRB may approve a request for a waiver or alteration of informed consent for non-FDA regulated studies if they meet the following criteria:

- The research involves no more than minimal risk to the participants;
- The research could not practicably be carried out without the waiver or alteration;
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver or alteration will not adversely affect the rights and welfare of the participants; and
- Whenever appropriate, the participants will be provided with additional pertinent information after participation.

C. Waiver of documentation of consent

A waiver of documentation of consent must meet the regulatory requirements of DHHS (45 CFR 46.117) and FDA (21 CFR 56.109). This may include an oral consent process or an electronic consent process by which a legally effective signature will not be obtained. The investigator should submit this request for waiver of documentation of consent with the study application and the investigator must include a script that the consent designee will use with participants or which will be made available electronically. This script must include all the required consent elements and the elements required for HIPAA privacy authorization (when PHI is to be collected). Details about that consent (time, date, identity of consent designee) should be recorded in the study record by the consent designee. If the project involves clinical care, these details about the consent should be added to the clinical record. Also note that since the HIPAA authorization would not be in writing, investigators should submit a HIPAA Form to request that the IRB grant an alteration to the HIPAA written signature requirement.

The IRB may approve a request for a waiver of documentation of consent for non-FDA regulated studies under three circumstances:

- The only record linking the participant to the research would be the consent document and, the principal risk to the participant would be potential harm resulting from a breach of confidentiality. In this case, each participant will be asked if he/she wants documentation linking him/her to the research and the participant's wishes will govern; or
- The research presents no more than minimal risk to the participants and involves no procedures for which written consent is normally required outside of the research context; or,
- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to

subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

For FDA-regulated studies, waiver of documentation is only permitted if the study presents no more than minimal risk (second bullet above).

If the IRB grants a waiver of documentation of consent, it may require the investigator to provide participants with a written statement regarding the research. Such a document requires IRB approval.

D. Describing the Informed Consent Process

i. Who may obtain informed consent?

The principal investigator for an IRB-approved research is ultimately responsible for the conduct of the study. Both the consent process and the consent form must be approved by the IRB. The principal investigator must ensure that informed consent from each potential research participant is:

1. obtained by an IRB approved consent designee, and
2. documented (if required) using the method approved by the IRB. Informed consent must be obtained before that participant takes part in any aspect of the research study, unless the IRB has approved a waiver of the requirement to obtain consent.

Investigators or study team members listed in the IRB application may obtain consent only after the approval of the IRB for each key research personnel. Each individual who interacts with potential research participants to obtain consent must complete submit transcripts for the CITI education requirement to the IRB as part of the application process.

The principal investigator must confirm that they have trained the individuals who will be getting consent. Each of these consenters must be knowledgeable about the study and must be capable of answering study-related questions posed by the potential participant.

Consenters must be “unconflicted”; they may not have a financial or outside conflict of interest associate with the research. Investigators with conflicts of interest must reports those conflicts to the IRB.

ii. When and where may informed consent be obtained?

The informed consent process description must include details about the timing and the place of informed consent. Depending on the type of study and the risk associated with it, participants should have adequate time to

review the consent form, ask questions about the research, and consult with family, friends or others (if desired) before signing the consent form.

NOTE: Consent should not be solicited immediately before beginning an elective procedure or scheduled therapy because the participant will not have time to consider whether or not to participate.

Generally, for research approved by TCH IRB, the consent form should be signed and include date and time of signature by both the participant and the principal investigator (or consent designee) at the time that consent is obtained. If the study involves sending the consent form to the potential participant for review and signature, without a face-to-face interaction with the consent designee, the process should describe whether there will be a telephone call to the individual to answer questions, and an explanation of the differences in the dates of the signatures of the participant and consent designee.

iii. From whom may consent/assent be obtained?

1. Adults

One of the ethical principles described in the Belmont Report, "Respect for Persons", provides that individuals should be treated as autonomous agents. This means that potential participants who are approached to volunteer to participate in a research study must be given sufficient information to allow them to make an informed decision about participation. In the US, adults (as defined by State law) may provide consent for themselves. In Ohio, adults are defined as persons age 18 or older. TCH does not participate in research involving children.

NOTE: Investigators who conduct research in which participants are recruited at sites outside of the State of Ohio must follow the law that applies in the local jurisdiction to determine who is an adult who may give legal consent, and how consent from adults who lack capacity should be obtained.

a. Adults who Lack Capacity to Provide Informed Consent

An exception to the general rule that an adult may consent for themself applies when an adult is determined to lack capacity to give consent. "Lack of capacity" to provide consent is not the same as "incompetence", and PIs of studies which seek to enroll adults who may lack capacity to make an informed decision must make clear in the IRB application how capacity to provide informed consent will be assessed. If participants are

expected to lose the ability to consent while the study progresses, explain procedures for reassessing the ability of participants to understand the protocol procedures and to provide ongoing informed consent.

Incompetence may be a temporary result of the participant's condition (e.g., the participant is unconscious or sedated) or may result from cognitive impairment produced by a disease or medical condition that impairs mental capacity. Whenever a participant lacks capacity to provide informed consent for him/herself, federal regulations require that the participant's ***legally authorized representative*** must give consent before the incapacitated person may participate in a research study.

For purposes of research conducted at The Christ Hospital, a ***legally authorized representative*** is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. Usually "the law of the jurisdiction in which the research is conducted" will be the state law where the research procedures will be performed.

Such consent may be obtained from a health care agent appointed by the person in a Durable Power of Attorney for Healthcare (DAHC) or similar document; court-appointed guardians for the person, or from next of kin in the following order of priority, unless otherwise specified in applicable law: spouse, adult child (18 years of age or older), parent, adult sibling (18 years of age or older), grandparent, or adult grandchild (18 years of age or older). NOTE: The preceding list contains the only surrogate entities who are allowed to provide consent for research purposes.

For individuals who know that they may lose capacity to provide consent during the course of the study, PIs should provide participants the opportunity to appoint a "research agent" who may provide consent on the participant's behalf after the participant loses capacity to consent for themself.

b. Other vulnerable adult populations
TCH IRB recognizes that the ability of adult populations to give voluntary informed consent may be compromised by circumstance. Those circumstances range from economic or educational disadvantage, physical handicap, sedation, and drug abuse to the terminally ill. The protocol should take into

account any of these issues and address them in the consent process.

c. Pregnant Women, Fetuses, and Neonates

Under the federal regulations, there are special conditions if pregnant women, fetuses or neonates will be involved in the research. (Note: “Neonates” are newborns who are not viable or whose viability is uncertain; healthy newborns are “children” under the regulations.) The conditions are listed at (45 CFR Subpart B). The pregnant woman must give her informed consent, and, if the research holds out the prospect of direct benefit only to the fetus, then the father must also give informed consent (unless he is unable to consent because of unavailability, incompetence, temporary incapacity, or the pregnancy resulted from rape or incest). Each individual providing consent must be informed of the impact of the research on the fetus.

d. Non-English Speakers

Federal regulations require that researchers obtain the legally effective informed consent of the research subjects or their legally authorized representative (if they are not able to consent for themselves). As a consequence, all information provided to potential subjects should be in a language that is understandable to those individuals. TCH IRB allows two means by which this can be accomplished- (1) Written translation of IRB-approved documents or (2) use of a Short Form and request for an exception.

The Principal Investigator must anticipate the need for written translations in considering the likely proportions of non-English-speaking people who may be encountered as eligible subjects for a proposed study. For instances of consenting an occasional and unexpected non-English-speaking subject in a study for which no consent form in the subject's language has been IRB-approved, the investigator must notify the IRB of the exception and utilize the IRB-approved short form consent in the subject’s language and an interpreter to translate the consent form in the subject’s language.

For purposes of research informed consent, an interpretation is a verbal exchange between two parties and the person serving as interpreter is fluent (can speak, read and write) in English and the language of the subject. A translation is the process of

translating a written document (e.g., consent form) from one language into another, assuring the language of the translated document has the same meaning as the written document in the first language.

iv. How does an investigator know if a participant understands the information in the consent form?

In order for participation in a study to be truly voluntary, the participant must understand what they are agreeing to do. The investigator must present the information to the participant in a way that is understandable to that participant, and then assess whether the participant did, indeed, understand the information. This part of the process is very important, because it lasts throughout the time that the participant is in the study. The investigator must make sure that the participant understands all the important elements of the consent form at the time the consent form is signed, and all during the research study. The participant must understand that participation is voluntary and that he or she can withdraw from the study at any time.

16.3 Basic Elements of Informed Consent

The Christ Hospital Institutional Review Board requires investigators to include the consent requirements established by DHHS (45 CFR 46.116) and FDA regulations (21 CFR 50.20), as applicable. These include the following nine required elements:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) For research involving more than minimal risk, an explanation as to whether

any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject;

(8) A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled; and

(9) One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or

(ii) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

If the research is subject to FDA regulation, a there must also be a statement that notes the possibility that the FDA may inspect study records (Research is FDA regulated if it involves the use of any drugs or medical devices other than the use of approved drugs and medical devices in the course of medical practice, or if the data will be submitted to or held for inspection by the FDA.)

In addition, the consent document may contain the following items when appropriate:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's or the legally authorized representative's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;

(5) A statement that significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects involved in the study;

(6) A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(7) A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and

(8) For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

These elements are included in the preprinted "boilerplate" text of the TCH IRB informed consent template.

In addition, the HIPAA authorization for use and disclosure of health information is included in the "boilerplate" text of the TCH IRB informed consent template. HIPAA, which took effect on April 14, 2003, requires a participant's prior written authorization before his or her identifiable health information can be used or disclosed by “covered entities”.

16.4 Informed Consent Documents that Require IRB Approval Prior to Use in a Study

The IRB must review and approval all materials associated with obtaining informed consent.